```
  1 GGCACGAGGAGATCTAGGTTCAAATTAATGTTGCCCCTAGTGGTAAAGGACAGAGACCCTCAGACTGATGAAATGCGCTCAGAATTACTT
 91 AGACAAAGCGGATATTTGCCACTCTCTTCCCCTTTTCCTGTGTTTTTGTAGTGAAGAGACCTGAAAGAAAAAAGTAGGGAGAACATAATG
                                                  *  *

181 AGAACAAATACGGTAATCTCTTCATTTGCTAGTTCAAGTGCTGGACTTGGGACTTAGGAGGGGCAATGGAGCCGCTTAGTGCCTACATCT
                                                     *

271 GACTTGGACTGAAATATAGGTGAGAGACAAGATTGTCTCATATCCGGGGAAATCATAACCTATGACTAGGACGGGAAGAGGAAGCACTGC
             *                                                    *

361 CTTTACTTCAGTGGGAATCTCGGCCTCAGCCTGCAAGCCAAGTGTTCACAGTGAGAAAAGCAAGAGAATAAGCTAATACTCCTGTCCTGA
                                                     *                                        *

451 ACAAGGCAGCGGCTCCTTGGTAAAGCTACTCCTTGATCGATCCTTTGCACCGGATTGTTCAAAGTGGACCCCAGGGGAGAAGTCGGAGCA
                                                  *

541 AAGAACTTACCACCAAGCAGTCCAAGAGGCCCAGAAGCAAACCTGGAGGTGAGACCCAAAGAAAGCTGGAACCATGCTGACTTTGTACAC
                                                                L  E  V  R  P  K  E  S  W  N  H  A  D  F  V  H      16

631 TGTGAGGACACAGAGTCTGTTCCTGGAAAGCCCAGTGTCAACGCAGATGAGGAAGTCGGAGGTCCcCAAATCTGCCGTGTATGTGGGGAC
    C  E  D  T  E  S  V  P  G  K  P  S  V  N  A  D  E  E  V  G  G  P  Q  I  C  R  V  C  G  D      46

721 AAGGCCACTGGCTATCACTTCAATGTCATGACATGTGAAGGATGCAAGGGCtTTTTCAGGAGGGCCATGAAACGCAACGCCCGGCTGAGG
    K  A  T  G  Y  H  F  N  V  M  T  C  E  G  C  K  G  F  F  R  R  A  M  K  R  N  A  R  L  R      76

811 TGCCCcTTCCGGAAGGGCGCCTGCGAGATCACCCGGAAGACCCGGCGACAGTGCCAGGCCTGCCGCCTGCGCAAGTGCCTGGAGAGCGGC
    C  P  F  R  K  G  A  C  E  I  T  R  K  T  R  R  Q  C  Q  A  C  R  L  R  K  C  L  E  S  G     106

901 ATGAAGAAGGAGATGATCATGTCCGACGAGGCCGTGGAGGAGAGGCGGGCCTTGATCAAGCGGAAGAAAAGTGAACGGACAGGGACTCAG
    M  K  K  E  M  I  M  S  D  E  A  V  E  E  R  R  A  L  I  K  R  K  K  S  E  R  T  G  T  Q     136
```

FIG. 1A

```
991 CCACTGGGAGTGCAGGGGCTGACAGAGGAGCAGCGGATGATGATCAGGGAGCTGATGGACGCTCAGATGAAAACCTTTGACACTACCTTC
    P  L  G  V  Q  G  L  T  E  E  Q  R  M  M  I  R  E  L  M  D  A  Q  M  K  T  F  D  T  T  F     166

1081 TCCCATTTCAAGAATTTCCGGCTGCCAGGGGTGCTTAGCAGTGGCTGCGAGTTGCCAGAGCCTCTGCAGGCCCCATCGAGGGAAGAAGCT
     S  H  F  K  N  F  R  L  P  G  V  L  S  S  G  C  E  L  P  E  P  L  Q  A  P  S  R  E  E  A     196

1171 GCCAAGTGGAGCCAGGTCCGGAAAGATCTGTGCTCTTTGAAGGTCTCTCTGCAAGCTGCGGGGGGAGGATGGCAGTGTCTGGAACTACAA
     A  K  W  S  Q  V  R  K  D  L  C  S  L  K  V  S  L  Q  A  A  G  G  G  W  Q  C  L  E  L  Q     226

1261 ACNCCCAGCCGACAGTGGCGGAAAGAGATCTTCTCCCTGCTGCCCCACATGGCTGACATGTCAACCTACATGTTCAAAGGCATCATCAGC
     T  P  S  R  Q  W  R  K  E  I  F  S  L  L  P  H  M  A  D  M  S  T  Y  M  F  K  G  I  I  S     256

1351 TTTGCCAAAGTCATCTCCTACTTCAGGGACTTGCCCATCGAGGACCAGATCTCCCTGCTGAAGGGGGCCGCTTTCGAGCTGTGTCAACTG
     F  A  K  V  I  S  Y  F  R  D  L  P  I  E  D  Q  I  S  L  L  K  G  A  A  F  E  L  C  Q  L     286

1441 AGATTCAACACAGTGTTCAACGCGGAGACTGGAACCTGGGAGTGTGGCCGGCTGTCCTACTGCTTGGAAGACACTGCAGGTGGCTTCCAG
     R  F  N  T  V  F  N  A  E  T  G  T  W  E  C  G  R  L  S  Y  C  L  E  D  T  A  G  G  F  Q     316

1531 CAACTTCTACTGGAGCCCATGCTGAAATTCCACTACATGCTGAAGAAGCTGCAGCTGCATGAGGAGGAGTATGTGCTGATGCAGGCCATC
     Q  L  L  L  E  P  M  L  K  F  H  Y  M  L  K  K  L  Q  L  H  E  E  E  Y  V  L  M  Q  A  I     346

1621 TCCCTCTTCTCCCCAGACCGCCCAGGTGTGCTGCAGCACCGCGTGGTGGACCAGCTGCAGGAGCAATTCGCCATTACTCTGAAGTCCTAC
     S  L  F  S  P  D  R  P  G  V  L  Q  H  R  V  V  D  Q  L  Q  E  Q  F  A  I  T  L  K  S  Y     376

1711 ATTGAATGCAATCGGCCCCAGCCTGCTCATAGGTTCTTGTTCCTGAAGATCATGGCTATGCTCACCGAGCTCCGCAGCATCAATGCTCAG
     I  E  C  N  R  P  Q  P  A  H  R  F  L  F  L  K  I  M  A  M  L  T  E  L  R  S  I  N  A  Q     406

1801 CACACCCAGCGGCTGCTGCGCATCCAGGACATACACCCCTTTGCTACGCCCCTCATGCAGGAGTTGTTCGGCATCACAGGTAGCTGAGCG
     H  T  Q  R  L  L  R  I  Q  D  I  H  P  F  A  T  P  L  M  Q  E  L  F  G  I  T  G  S  *        434

1891 GCTGCCTTGGGTGACACCTTCGAGAGGCAGCCAGACCCAGAGCCCTCTGAGCCGGCACTCCCGGGCCAAGACAGATGGACACTGCCAAGA
1981 GCCGACAATGCCCTGCTGGCCTGTCTCCCTAGGGAATTCCTGCTATGACAGCTGGCTAGCATTCCTCAGGAAGGACATGGGGTGCCCC  2068
```

FIG. 1B

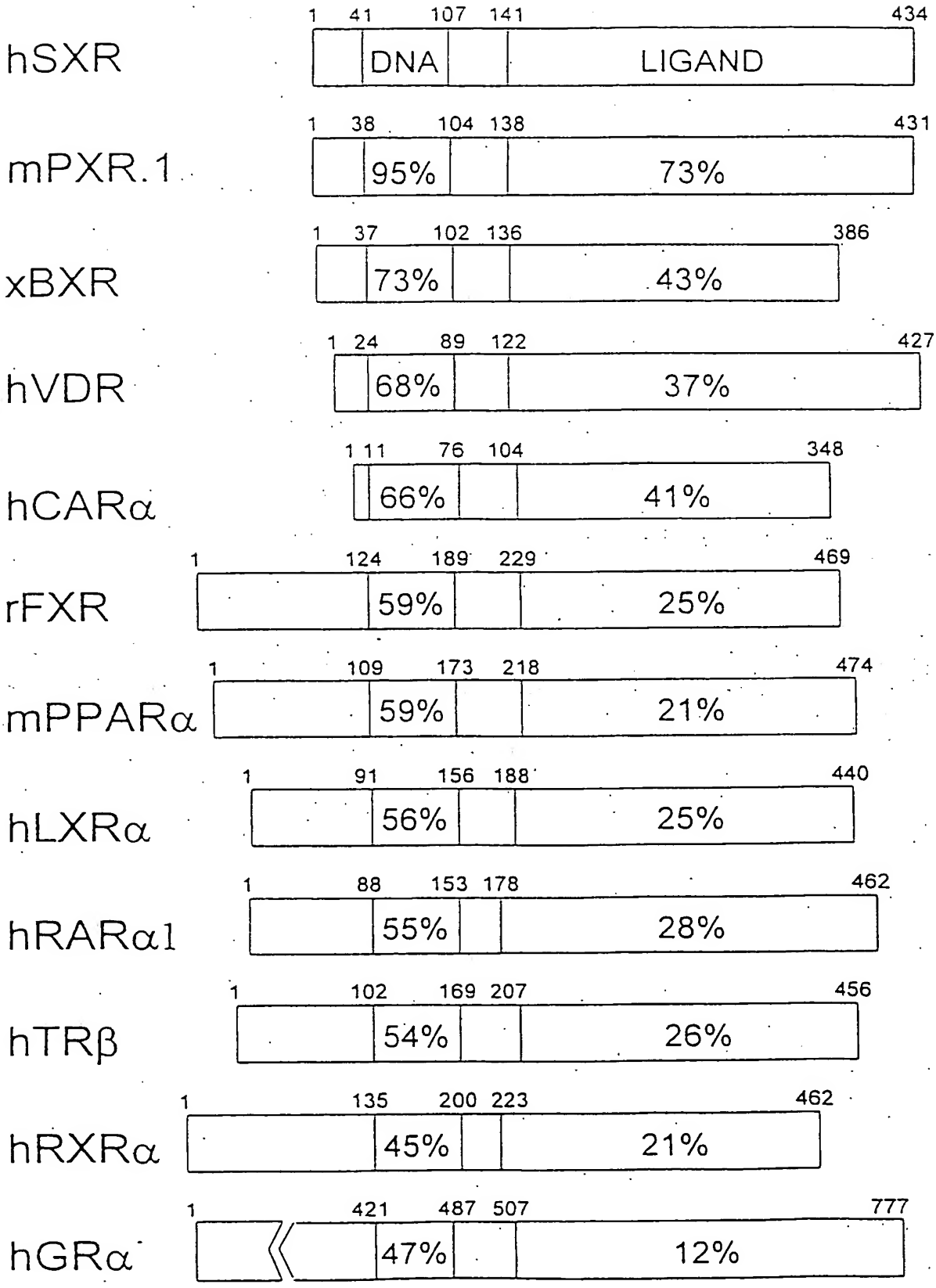
hSXR
1 41 107 141 434
DNA
LIGAND
mPXR.1
1 38 104 138 431
95%
73%
xBXR
1 37 102 136 386
73%
43%
hVDR
1 24 89 122 427
68%
37%
hCARα
1 11 76 104 348
66%
41%
rFXR
1 124 189 229 469
59%
25%
mPPARα
1 109 173 218 474
59%
21%
hLXRα
1 91 156 188 440
56%
25%
hRARα1
1 88 153 178 462
55%
28%
hTRβ
1 102 169 207 456
54%
26%
hRXRα
1 135 200 223 462
45%
21%
hGRα
1 421 487 507 777
47%
12%

FIG. 1C

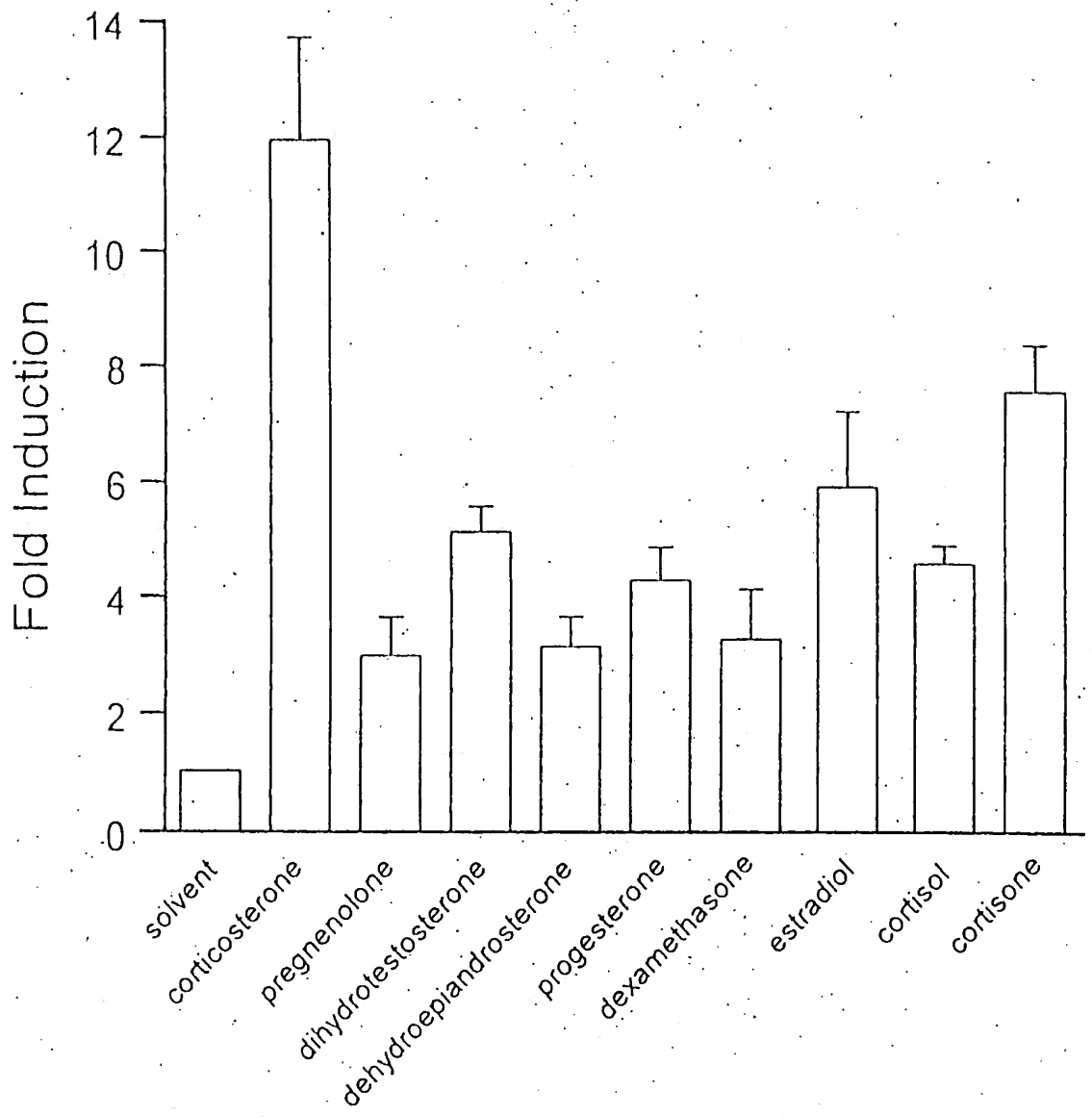
Fold Induction
14
12
10
8
6
4
2
0
solvent
corticosterone
pregnenolone
dihydrotestosterone
dehydroepiandrosterone
progesterone
dexamethasone
estradiol
cortisol
cortisone

FIG. 2

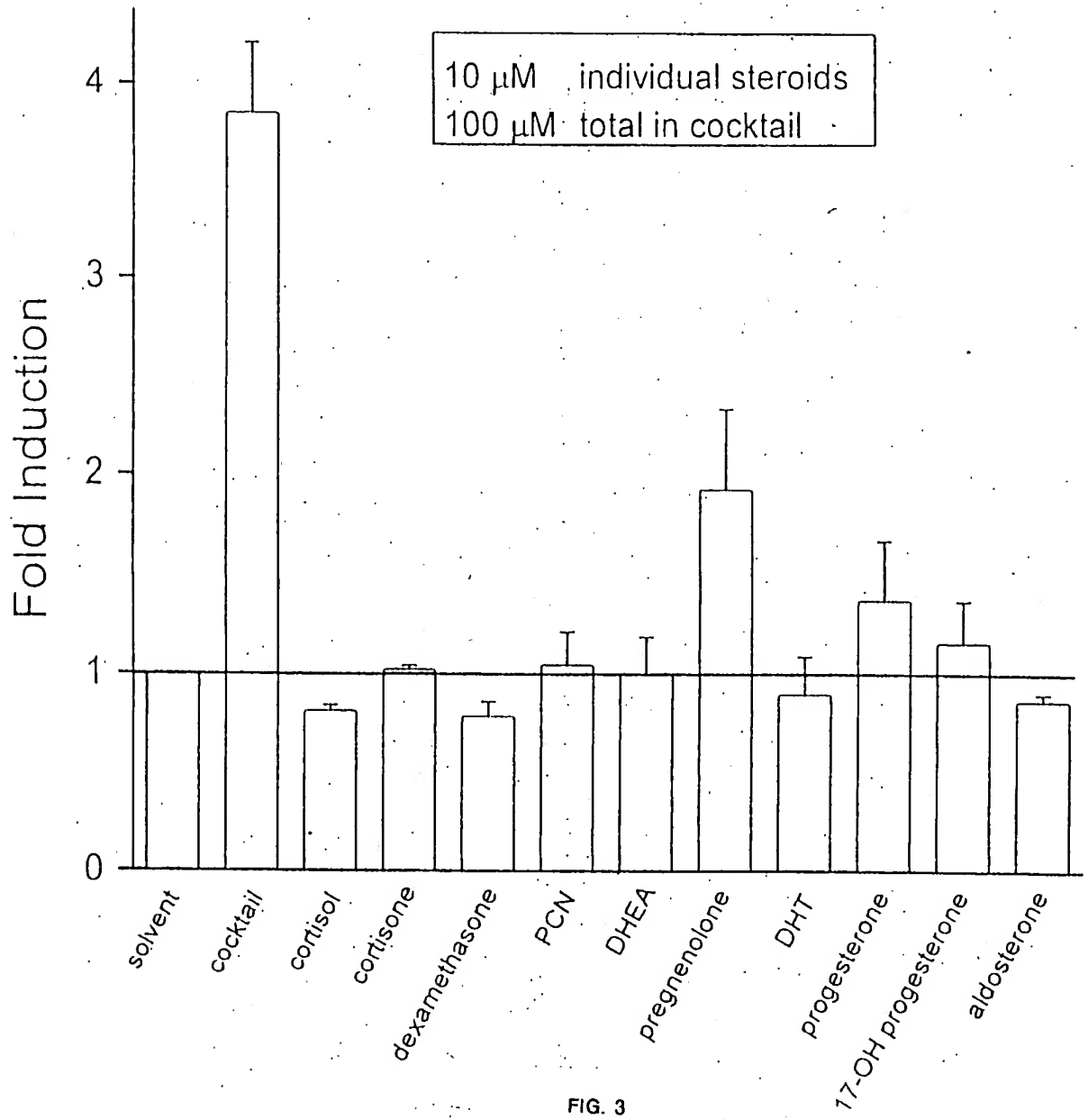
10 μM individual steroids
100 μM total in cocktail
Fold Induction
0
1
2
3
4
solvent
cocktail
cortisol
cortisone
dexamethasone
PCN
DHEA
pregnenolone
DHT
progesterone
17-OH progesterone
aldosterone

FIG. 3

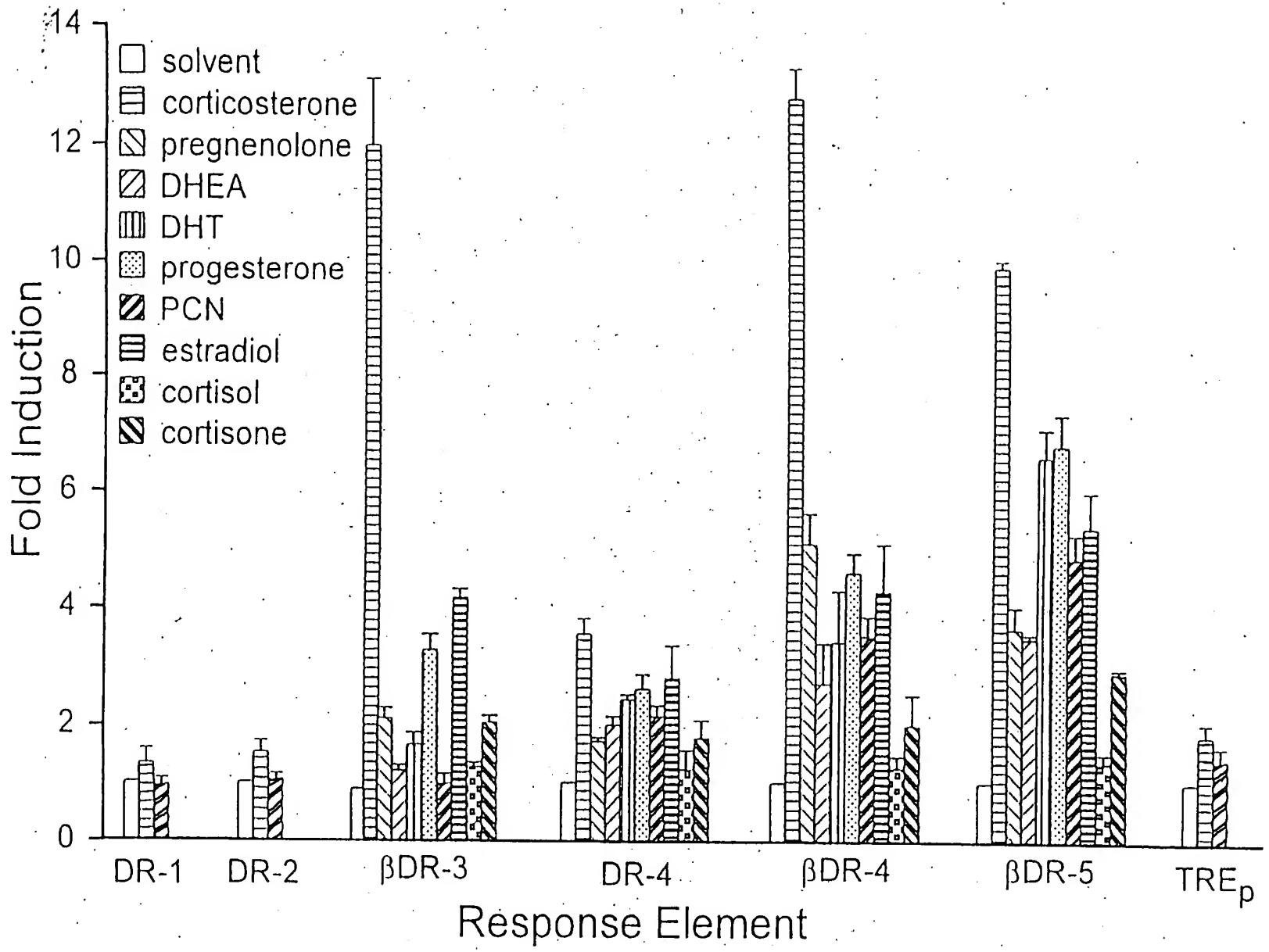
14
12
10
8
6
4
2
0
Fold Induction
solvent
corticosterone
pregnenolone
DHEA
DHT
progesterone
PCN
estradiol
cortisol
cortisone
DR-1
DR-2
βDR-3
DR-4
βDR-4
βDR-5
TREp
Response Element

FIG. 4

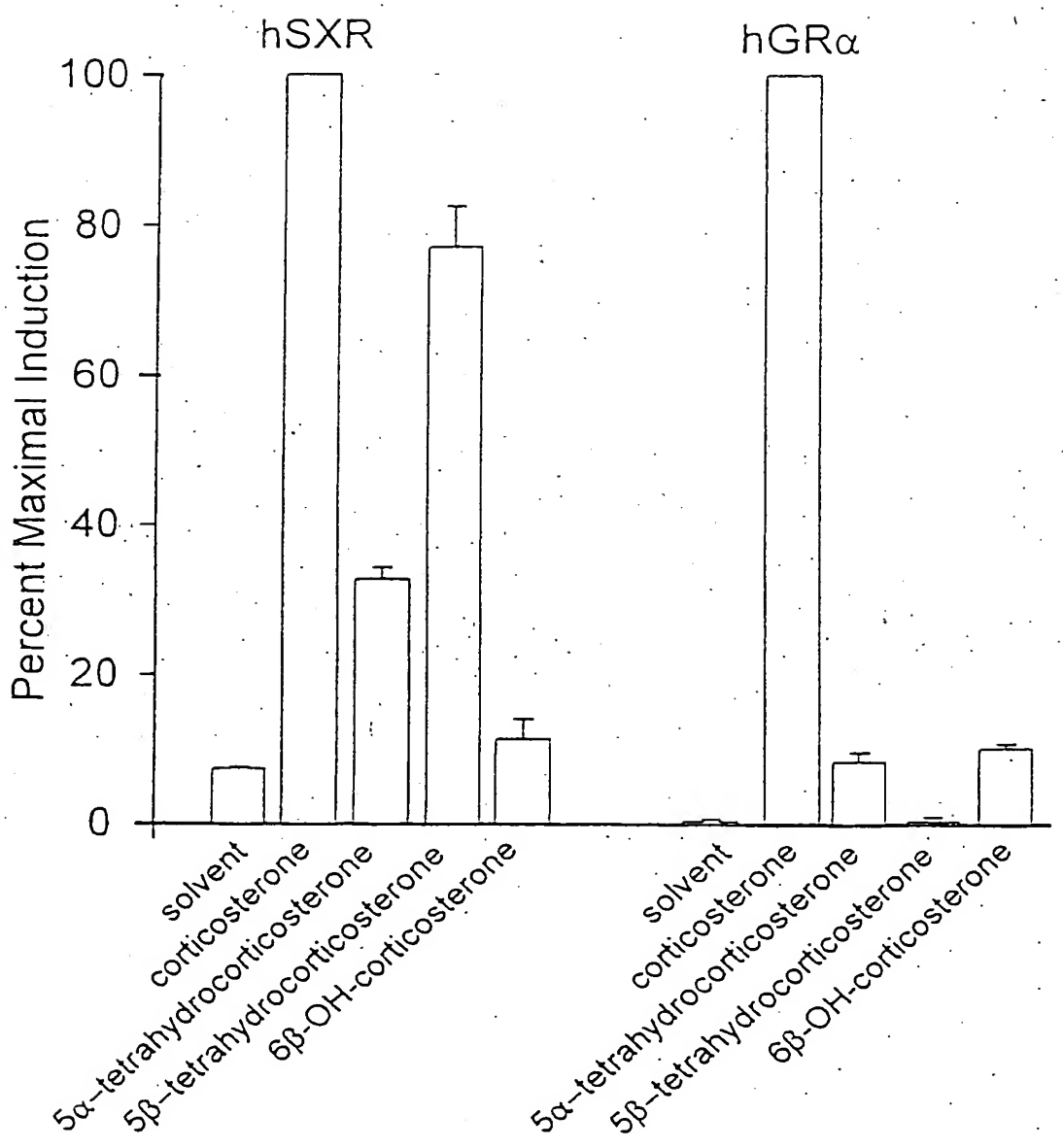
hSXR
hGRα
Percent Maximal Induction
100
80
60
40
20
0
solvent
corticosterone
5α–tetrahydrocorticosterone
5β–tetrahydrocorticosterone
6β-OH-corticosterone
solvent
corticosterone
5α–tetrahydrocorticosterone
5β–tetrahydrocorticosterone
6β-OH-corticosterone

FIG. 5

DR-3

rCYP3A1	tagac AGTTCA tga AGTTCA tctac
rCYP3A2	taagc AGTTCA taa AGTTCA tctac
rUGT1A6	actgt AGTTCA taa AGTTCA catgg

DR-4

rbCYP2C1	caatc AGTTCA acag GGTTCA ccaat
rP450R	cac AGGTGA gctg AGGCCA gcagc AGGTCG aaa

DR-5

rCYP2A1	gtgca GGTTCA actgg AGGTCA acatg
rCYP2A2	gtgct GGTTCA actgg AGGTCA gtatg
rCYP2C6	agtct AGTTCA gtggg GGTTCA gtctt
hCYP2E1	gagat GGTTCA aggaa GGGTCA ttaac

FIG. 6A

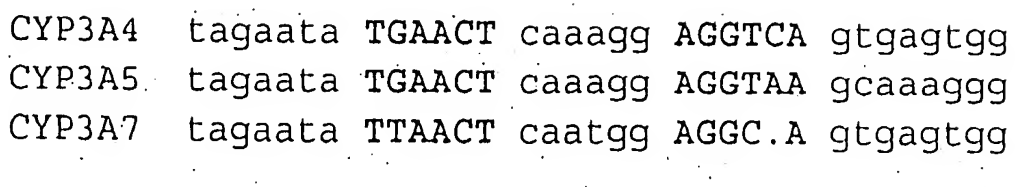
CYP3A4 tagaata TGAACT caaagg AGGTCA gtgagtgg
CYP3A5 tagaata TGAACT caaagg AGGTAA gcaaaggg
CYP3A7 tagaata TTAACT caatgg AGGC.A gtgagtgg

FIG. 6B

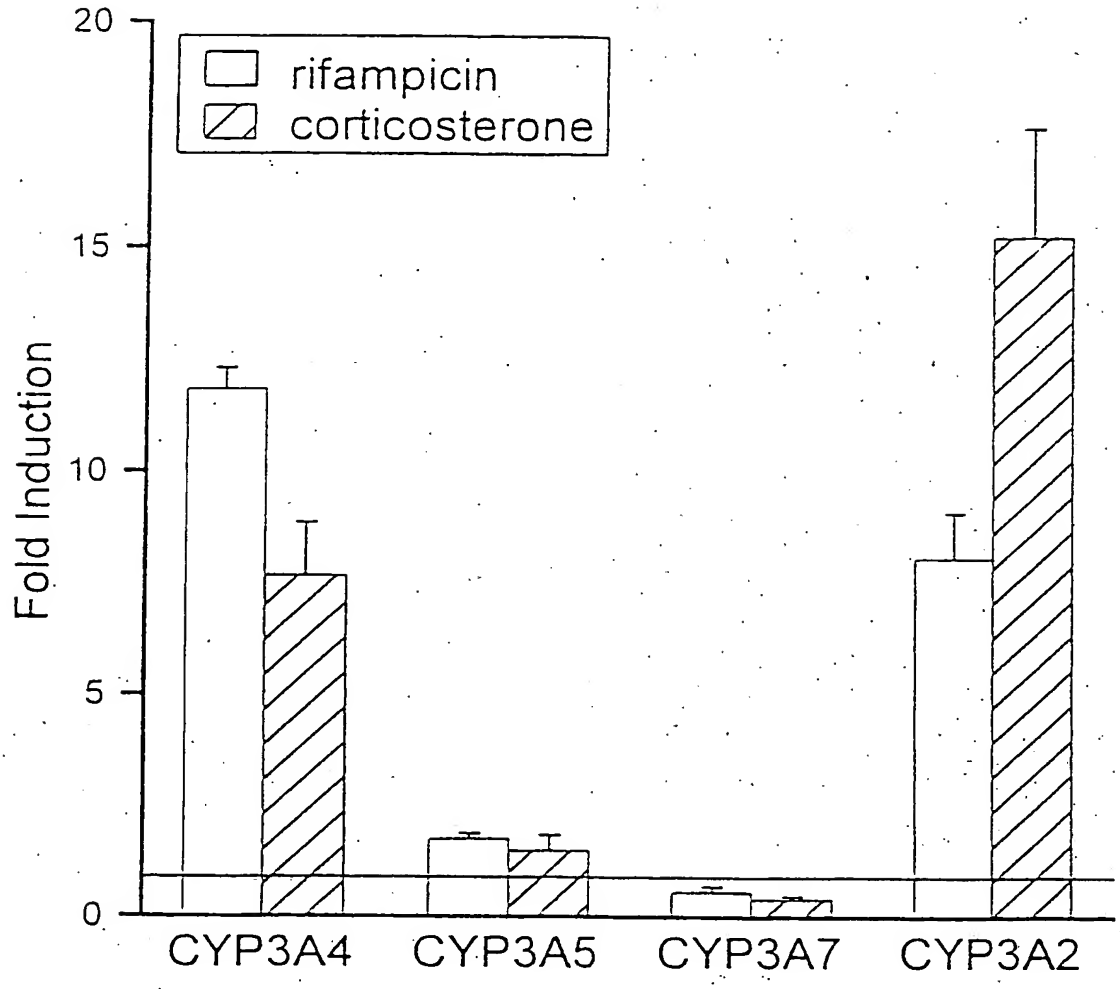
20
15
10
5
0
Fold Induction
rifampicin
corticosterone
CYP3A4
CYP3A5
CYP3A7
CYP3A2

FIG. 6C

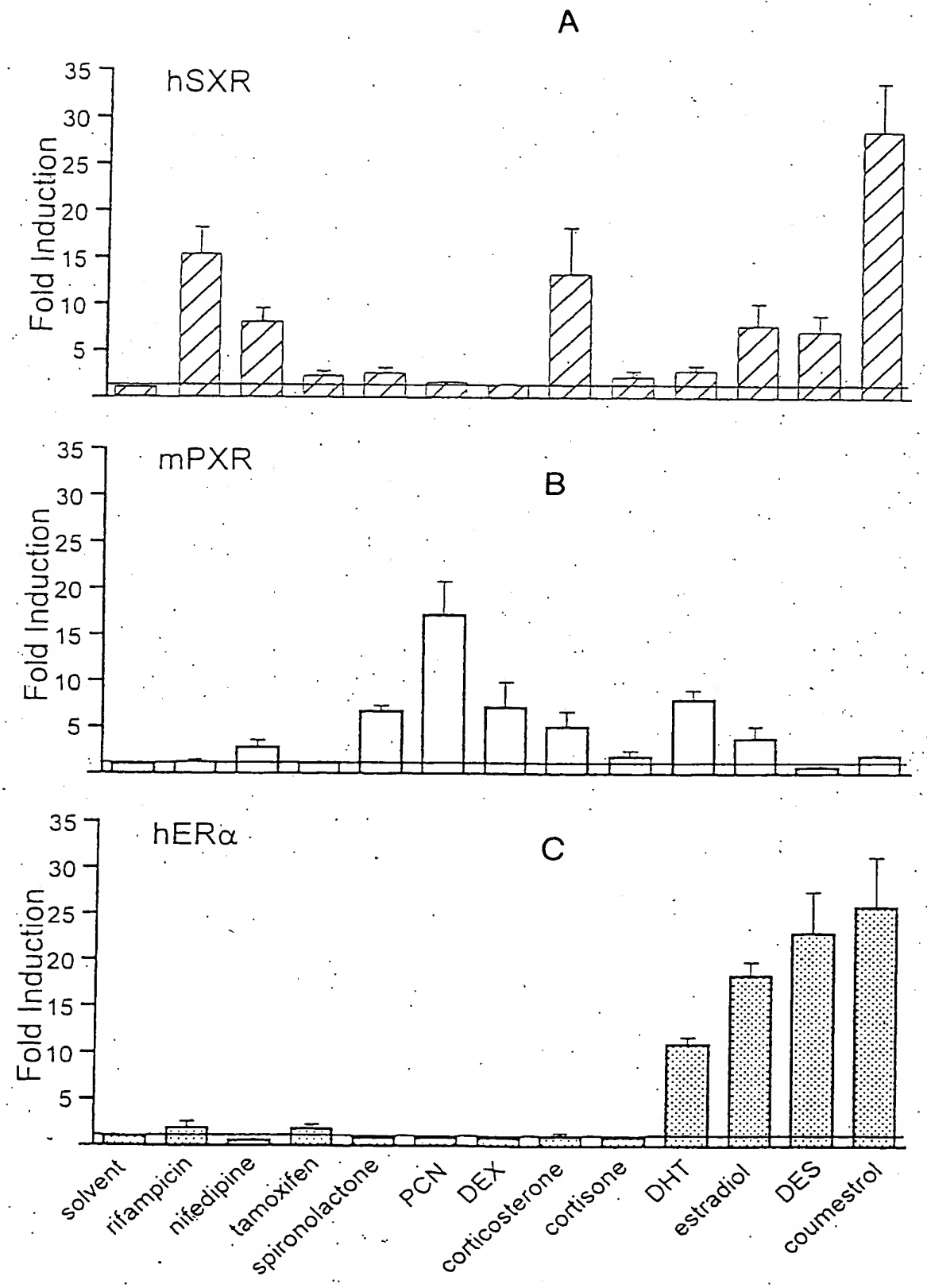
A
hSXR
Fold Induction
35
30
25
20
15
10
5
B
mPXR
Fold Induction
C
hERα
Fold Induction
solvent
rifampicin
nifedipine
tamoxifen
spironolactone
PCN
DEX
corticosterone
cortisone
DHT
estradiol
DES
coumestrol

FIG. 7

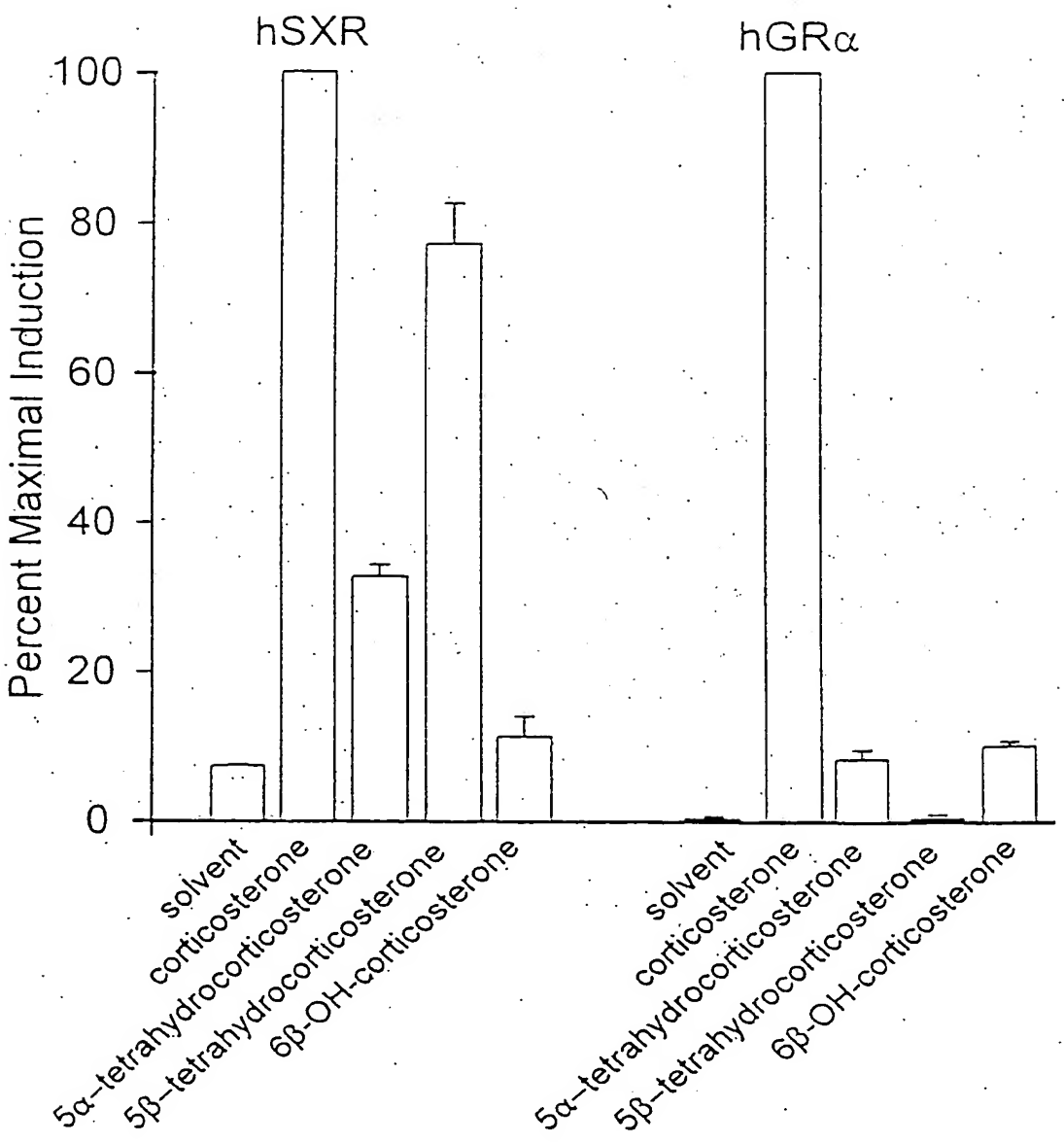
hSXR
hGRα
Percent Maximal Induction
100
80
60
40
20
0
solvent
corticosterone
5α–tetrahydrocorticosterone
5β–tetrahydrocorticosterone
6β-OH-corticosterone
solvent
corticosterone
5α–tetrahydrocorticosterone
5β–tetrahydrocorticosterone
6β-OH-corticosterone

FIG. 7D

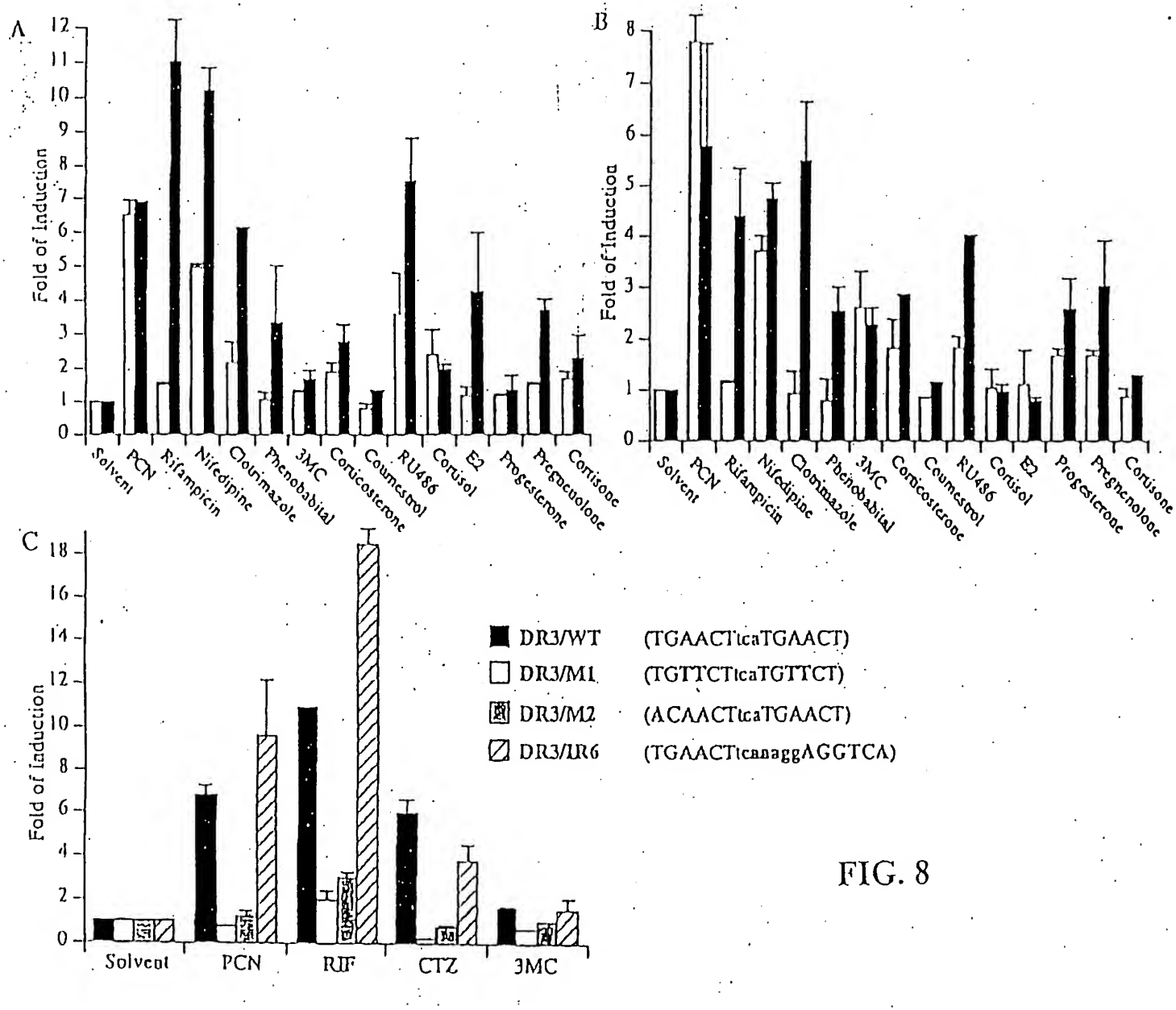
A
Fold of Induction
Solvent
PCN
Rifampicin
Nifedipine
Clotrimazole
Phenobabital
3MC
Corticosterone
Coumestrol
RU486
Cortisol
E2
Progesterone
Pregnenolone
Cortisone
B
Fold of Induction
Solvent
PCN
Rifampicin
Nifedipine
Clotrimazole
Phenobabital
3MC
Corticosterone
Coumestrol
RU486
Cortisol
E2
Progesterone
Pregnenolone
Cortisone
C
Fold of Induction
Solvent
PCN
RIF
CTZ
3MC
DR3/WT (TGAACTtcaTGAACT)
DR3/M1 (TGTTCTtcaTGTTCT)
DR3/M2 (ACAACTtcaTGAACT)
DR3/IR6 (TGAACTtcaaggAGGTCA)

FIG. 8

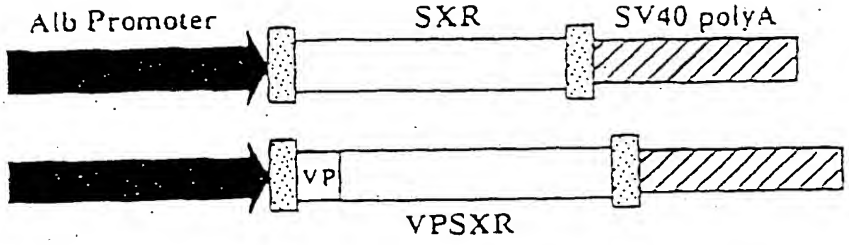
Alb Promoter
SXR
SV40 polyA
VP
VPSXR

FIG. 9

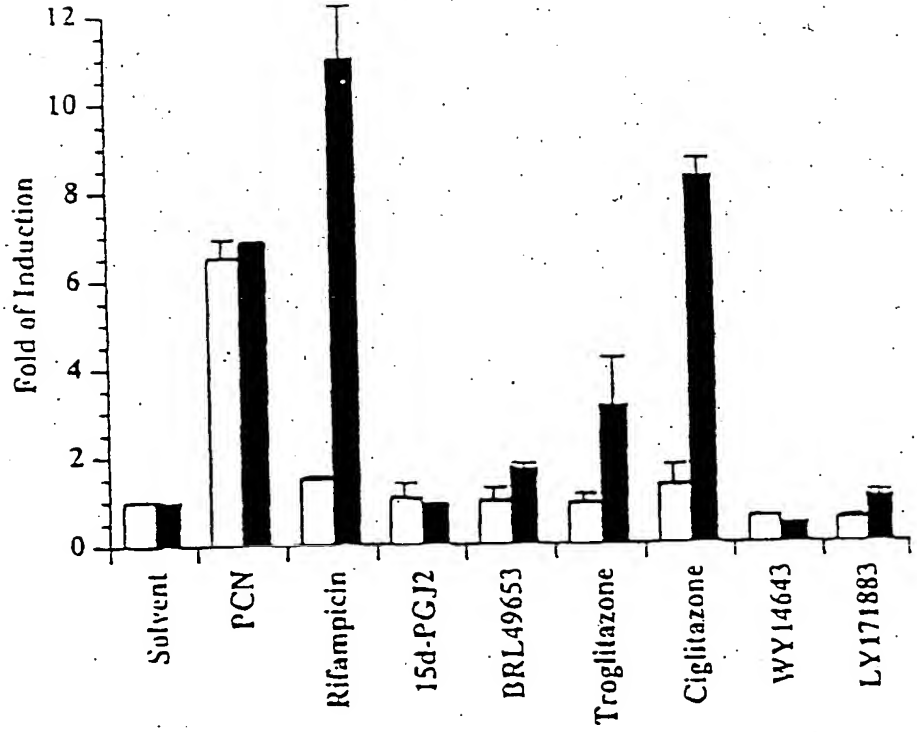
Fold of Induction
0
2
4
6
8
10
12
Solvent
PCN
Rifampicin
15d-PGJ2
BRL49653
Troglitazone
Ciglitazone
WY14643
LY171883

FIG. 10

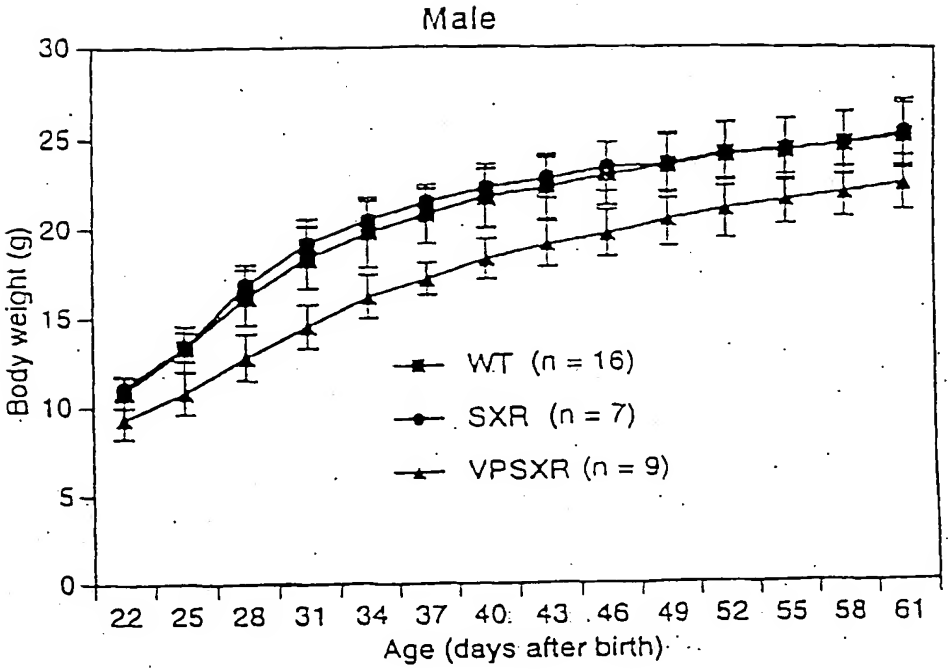
Male
Body weight (g)
30
25
20
15
10
5
0
22 25 28 31 34 37 40 43 46 49 52 55 58 61
Age (days after birth)
WT (n = 16)
SXR (n = 7)
VPSXR (n = 9)

FIG. 11

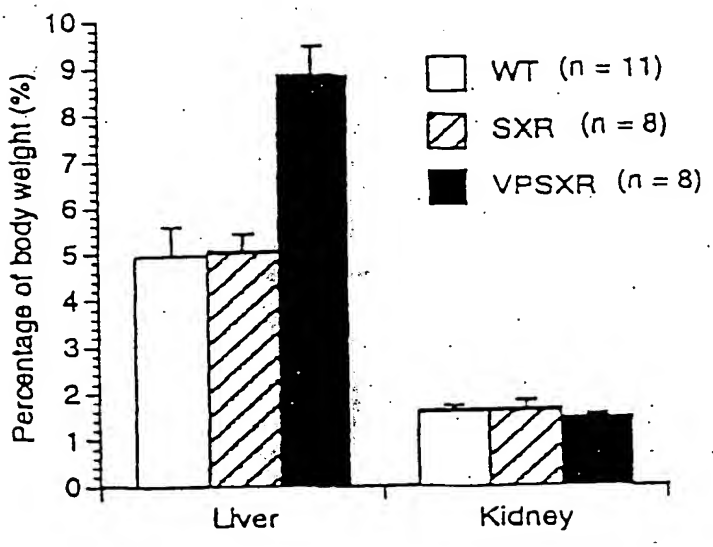
Percentage of body weight (%)
10
9
8
7
6
5
4
3
2
1
0
Liver
Kidney
WT (n = 11)
SXR (n = 8)
VPSXR (n = 8)

FIG. 12